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NOTICE OF ALLOWANCE AND FEE(S) DUE

7590

12/16/2002

Jill A. Fahrlander Michael Best & Friedrich One South Pinckney Street P.O. Box 1806 Madison, WI 53701-1806

EXAMINER			
SOUAYA	SOUAYA, JEHANNE E		
ART UNIT	CLASS-SUBCLASS		
1634	514-100000		

DATE MAILED: 12/16/2002

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/538,338	03/29/2000	Steven Albert Benner	13238.9USC1	6192

TITLE OF INVENTION: METHODS FOR PREPARING OLIGONUCLEOTIDES CONTAINING NON-STANDARD NUCLEOTIDES

A PRICAL MAINE					
APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$640	\$0	\$640	03/17/2003

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

- A. Pay TOTAL FEE(S) DUE shown above, or
- B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.
- Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.



PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Commissioner for Patents Washington, D.C. 20231

(703)746-4000 <u>Fax</u>

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks I through 4 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and (a) the indication of the current correspondence address in Block 1, by (b) indicating a new correspondence address; and (b) indicating a new correspondence address; and (c) the indicating a new correspondence address and (c) the indicating a new corre

maintenance fee notification	ns.			orrespondence addr	ess; and/or (b) indicating a sepa	trate "FEE ADDRESS" for
CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use Block 7590 12/16/2002 Jill A. Fahrlander			Block I)	Note: A certificat Fee(s) Transmit accompanying pa formal drawing, r	e of mailing can only be used fo tal. This certificate cannot apers. Each additional paper, s nust have its own certificate of n	r domestic mailings of the be used for any other uch as an assignment or nailing or transmission.
Michael Best & Fr					Certificate of Mailing or Trans	imission
One South Pinckne	ey Street			I hereby certify United States Pos	that this Fcc(s) Transmittal is	being deposited with the
P.O. Box 1806 Madison, WI 5370	1-1806			envelope address	that this Fec(s) Transmittal is tal Service with sufficient postaged to the Box Issue Fee address USPTO, on the date indicated b	above, or being facsimile elow.
,		•				(Depositor's name)
						(Signature)
						(Date)
APPLICATION NO.	FILING DATE	FIRS	ST NAMED INVEN	TOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/538,338	03/29/2000		teven Albert Ben		13238.9USC1	6192
TITLE OF INVENTION: M						
APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBL	JICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$640		\$0	\$640	03/17/2003
EXAMI		ART UNIT	CLASS-SUBC	LASS		
SOUAYA, JE	HANNE E	1634	514-1000	00		
1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363). 2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered						
The Company of the second of t						
		low, no assignee data wi submitted under separate	ill appear on the cover. Completic	•• •	assignee data is only appropriate of a substitute for filing an assig OUNTRY)	e when an assignment has nment.
Please check the appropriate	assignee category or category	gories (will not be printed	on the patent)	individual u	corporation or other private gr	oup entity
la. The following fee(s) are	enclosed:	4b. Pay	ment of Fee(s):			
☐ Issue Fee ☐ A check		eck in the amoun	t of the fec(s) is enc	losed.		
		•	d. Form PTO-2038			
□ Advance Order - # of Copies □ The Commissioner is hereby authorized by charge the required fee(s), or credit any overpayment, Deposit Account Number (enclose an extra copy of this form).			redit any overpayment, to orm).			
Commissioner for Patents is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above.						
Authorized Signature)		(Date)				
NOTE; The Issue Fee and Publication Fee (if required) will not be accepted other than the applicant; a registered attorney or agent; or the assignee or o interest as shown by the records of the United States Patent and Trademark Office		r other party in				
This collection of informa obtain or retain a benefit application. Confidentiality estimated to take 12 minut completed application for case. Any comments on suggestions for reducing t Patent and Trademark Off NOT SEND FEES OR Commissioner for Patents,	tion is required by 37 CF by the public which is U.S.C, y is governed by 35 U.S.C, les to complete, including m to the USPTO. Time v the amount of time you his burden, should be sen ice, U.S. Department of C COMPLETED FORMS Washington, DC 20231.	R 1.311. The information file (and by the USPTC 1.22 and 37 CFR 1.14. To gathering, preparing, and will vary depending upon require to complete the tothe Chief Information ommerce, Washington, ISTO THIS ADDRES	on is required to to process) an in its collection is disubmitting the in the individual his form and/or on Officer, U.S. D.C. 20231. DOS. SEND TO:			
Under the Paperwork Re collection of information u	duction Act of 1995, no	persons are required t				



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7	590 12/16/2002	[EXAMIN	ER
Jill A. Fahrlander			SOUAYA, JEI	HANNE E
Michael Best & Fr One South Pinckno		[ART UNIT	PAPER NUMBER
P.O. Box 1806 Madison, WI 5370	1 1906		1634	
UNITED STATES		I	DATE MAILED: 12/16/2002	

Determination of Patent Term Extension under 35 U.S.C. 154 (b) (application filed after June 7, 1995 but prior to May 29, 2000)

The patent term extension is 0 days. Any patent to issue from the above identified application will include an indication of the 0 day extension on the front page.

If a continued prosecution application (CPA) was filed in the above-identified application, the filing date that determines patent term extension is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system. (http://pair.uspto.gov)

Any questions regarding the patent term extension or adjustment determination should be directed to the Office of Patent Legal Administration at (703)305-1383.



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Jill A. Fahrlander		SOUAYA, JEHANNE E		
Michael Best & Fr				
One South Pinckno	ey Street		ART UNIT	PAPER NUMBER
P.O. Box 1806			1634	
Madison, WI 5370	1-1806			
UNITED STATES			DATE MAILED: 12/16/2002	

Notice of Fee Increase on January 1, 2003

If a reply to a "Notice of Allowance and Fee(s) Due" is filed in the Office on or after January 1, 2003, then the amount due will be higher than that set forth in the "Notice of Allowance and Fee(s) Due" since there will be an increase in fees effective on January 1, 2003. See Revision of Patent and Trademark Fees for Fiscal Year 2003; Final Rule, 67 Fed. Reg. 70847, 70849 (November 27, 2002).

The current fee schedule is accessible from: http://www.uspto.gov/main/howtofees.htm.

If the issue fee paid is the amount shown on the "Notice of Allowance and Fee(s) Due," but not the correct amount in view of the fee increase, a "Notice to Pay Balance of Issue Fee" will be mailed to applicant. In order to avoid processing delays associated with mailing of a "Notice to Pay Balance of Issue Fee," if the response to the Notice of Allowance and Fee(s) due form is to be filed on or after January 1, 2003 (or mailed with a certificate of mailing on or after January 1, 2003), the issue fee paid should be the fee that is required at the time the fee is paid. If the issue fee was previously paid, and the response to the "Notice of Allowance and Fee(s) Due" includes a request to apply a previously-paid issue fee to the issue fee now due, then the difference between the issue fee amount at the time the response is filed and the previously paid issue fee should be paid. See Manual of Patent Examining Procedure, Section 1308.01 (Eighth Edition, August 2001).

Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

Notice of Allowability

Application No. **09/538,338**

Applicant(s)

Steven Benner

Examiner

Jehanne Souaya

Art Unit 1634



The MAILING DATE of this communication appears on the co	over sheet with the correspondence address			
All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.				
1. \boxtimes This communication is responsive to <u>the proposed amendment</u>	filed 12/4/2002 .			
2. X The allowed claim(s) is/are 6 and 12-14				
3. The drawings filed on are accepted by the gradient of the gradient	ne Examiner.			
4. \square Acknowledgement is made of a claim for foreign priority under	35 U.S.C. § 119(a)-(d).			
a) \square All b) \square Some* c) \square None of the:				
1. \square Certified copies of the priority documents have been rece	eived.			
2. \square Certified copies of the priority documents have been rece	eived in Application No			
 Copies of the certified copies of the priority documents happlication from the International Bureau (PCT Rule 17) *Certified copies not received: 	7.2(a)).			
5. Acknowledgement is made of a claim for domestic priority under				
(a) The translation of the foreign language provisional application				
6. X Acknowledgement is made of a claim for domestic priority und	•			
Applicant has THREE MONTHS FROM THE "MAILING DATE" of this commoted below. Failure to timely comply will result in ABANDONMENT of the EXTENDABLE.	unication to file a reply complying with the requirements is application. THIS THREE-MONTH PERIOD IS NOT			
7. A SUBSTITUTE OATH OR DECLARATION must be submitted. Note to INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s)	the attached EXAMINER'S AMENDMENT or NOTICE OF why the oath or declaration is deficient.			
8. X CORRECTED DRAWINGS must be submitted.	· .			
(a) \boxtimes including changes required by the Notice of Draftsperson's 1) \boxtimes hereto or 2) \square to Paper No	•			
(b) \square including changes required by the proposed drawing correct approved by the examiner.	cion filed, which has been			
(c) \square including changes required by the attached Examiner's Ame Paper No	endment/Comment or in the Office action of			
Identifying indicia such as the application number (see 37 CFR 1.84(c)) should each sheet. The drawings should be filed as a separate paper with a transmit	be written on the drawings in the top margin (not the back) of tal letter addressed to the Official Draftsperson.			
9. DEPOSIT OF and/or INFORMATION about the deposit of BIOLOG attached Examiner's comment regarding REQUIREMENT FOR THE				
Attachment(s)				
1 Notice of References Cited (PTO-892)	2 Notice of Informal Patent Application (PTO-152)			
3 X Notice of Draftsperson's Patent Drawing Review (PTO-948) 5 Information Disclosure Statement(s) (PTO-1449), Paper No(s).	4 X Interview Summary (PTO-413), Paper No. <u>17</u> .			
 Information Disclosure Statement(s) (PTO-1449), Paper No(s). Examiner's Comment Regarding Requirement for Deposit of Biological 	6 X Examiner's Amendment/Comment 8 X Examiner's Statement of Reasons for Allowance			
Material	- Lacinion of Statement of Househis for Allowalide			
9 Other				

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EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Jill Fahrlander on 12/11/2002.

- 2. The application has been amended as follows:
- In claim 12, line 15, delete the recitation of "comprises" and insert instead -- is performed with--.
 - In claim 12, line 15, delete the recitation of "DNA".
- In claim 12, line 16, delete the recitation of "T4 DNA polymerase,".
- In claim 13, line 1, delete the recitation of "DNA".
- ✓ In claim 13, line 1, delete the recitation of "comprises" and insert instead --is--.
- In claim 14, line 16, delete the recitation of "comprises" and insert instead -- is performed with--.

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REASONS FOR ALLOWANCE

3. The following is an examiner's statement of reasons for allowance: The claims are drawn to a method of making an oligonucleotide comprising a template oligonucleotide comprising a sequence of nucleotides wherein the template comprises at least one non standard nucleotide at a preselected site in the sequence, wherein the non standard nucleotide is iso-G or iso-C; contacting the template with a mixture of nucleotide triphosphates, the mixture comprising nucleotide triphosphates that are complementary to the nucleotides in the template, wherein the nucleotide triphosphate complementary to the non standard nucleotide at the preselected site comprises a derivatized nucleotide; and forming an oligonucleotide complementary to a portion of the template by enzymatic polymerization of the nucleotides triphosphates in a sequence complementary to a portion of the template. The claims are also drawn to a method of making an oligonucleotide comprising a template oligonucleotide comprising a sequence of nucleotides wherein the template comprises at least one non standard nucleotide at a preselected site in the sequence; contacting the template with a mixture of nucleotide triphosphates, the mixture comprising nucleotide triphosphates that are complementary to the nucleotides in the template, wherein the nucleotide triphosphate complementary to the non standard nucleotide at the preselected site comprises a derivatized nucleotide; and forming an oligonucleotide complementary to a portion of the template by enzymatic polymerization of the nucleotide triphosphates in a sequence complementary to a portion of the template, wherein the enzymatic polymerization is performed with AMV reverse transcriptase or Klenow Fragment of DNA

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polymerase I. The claims are further drawn to a method of making an oligonucleotide comprising a template oligonucleotide comprising a sequence of nucleotides wherein the template comprises at least one non standard nucleotide at a preselected site in the sequence; contacting the template with a mixture of nucleotide triphosphates, the mixture comprising nucleotide triphosphates that are complementary to the nucleotides in the template, wherein the nucleotide triphosphate complementary to the non standard nucleotide at the preselected site comprises a derivatized nucleotide comprising radiolabel; and forming an oligonucleotide complementary to a portion of the template by enzymatic polymerization of the nucleotides triphosphates in a sequence complementary to a portion of the template, wherein the enzymatic polymerization is performed with T7 RNA polymerase.

The closest prior art is that of Eritja et al., (Nucleic Acids Research, 1986; 14(20), pp 8135-8153) which teaches a method for making an oligonucleotide using a template containing xanthine and contacting the template with a mixture of nucleotide triphosphates including 9-(β --D-2'-deoxyribofuranosyl)-2-aminopurine triphosphate (dAPTP) and Drosophila polymerase α to form an oligonucleotide complementary to the template (dATPT is also incorporated in the oligonucleotide opposite xanthine in the template). The claims are allowable over the prior art of Eritja et al because Eritja et al do not teach using iso-G or iso-C either in the template or as a derivatized nucleotide triphosphate, nor does Eritja teach forming an oligonucleotide with Klenow fragment of DNA polymerase I, AMV reverse transcriptase or T7 RNA polymerase. Eritja et al teach away from using Klenow fragment because Eritja et al teach that when Klenow

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fragment was used as the polymerase, which has 3' exonuclease activity, removal of the nucleotide opposite xanthine and extensive degradation of the primer was observed (p. 8142, last para). Therefore, Eritja et al does not teach a reasonable explanation of success that any polymerase, such as T7 RNA polymerase, Klenow fragment of DNA polymerase I (which the specification teaches were successful in the instantly claimed methods), or AMV reverse transcriptase would be capable of use in the method of Eritja et al.

4. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya Patent examiner

Art Unit 1634

Jehanne Sovaya

JEHANNE SOUAYA
PATENT EXAMINER